ABSTRACT

The invention concerns the identification of a pathway where the co-receptor CD28 inactivates glycogen synthase 3 (GSK-3) and where a reagent that inhibits GSK-3 can enhance, or substitute for CD28-dependent T-cell mediated immune responses. Altered T-cell responses are applied to increased proliferation, cytokine production and in the generation of increased cytolytic T-cell responses (CTLs) in the context of infection by virus', bacterial, fungi or prions. For example, the use of GSK-3 inhibitor SB415286 preferentially cooperated with CD28 costimulation to increase interleukin 2 (IL-2) transcription, and to provide CD28-replacement signals leading to increased IL-2 transcription. Similarly, inhibitors SB415286 and lithium chloride increased the CD28-dependent generation of cytolytic T-cell responses (CTLs) against a virally or baterially infected cells. Overall, the invention relates to a CD28 induced signaling transduction pathway that inactivates glycogen synthase kinase (GSK) and the application of this finding to the modulation of T-cell activation, proliferation and the generation of cytolytic T-cells (CTLs).